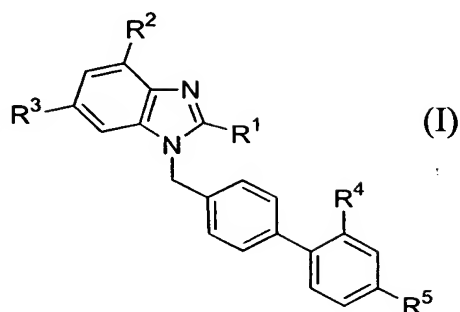


## CLAIMS

*What is Claimed Is:*

- 5 1. A compound of the structure:



10 wherein  $R^1$ ,  $R^2$ , and  $R^3$  independently are hydrogen, hydroxy, halo, amino alkylamino, dialkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy, thiocarboxy, carbamoyl, cyano, hydroxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, alkyl, alkenyl, alkynyl, aryl, 5- or 6- membered heterocyclic ring, or a fused 2-, 3-, or 4-membered heterocyclic radical;

15  $R^4$  and  $R^5$  independently are hydrogen, cyanate, or a negatively charged group.

2. The compound of claim 1, wherein:

$R^1$  is hydrogen, halogen, methoxy, hydroxyl, methyl, ethyl, or  $\text{NH}_2$ ;

$R^2$  is lower alkyl;

20  $R^3$  is phenyl, a fused 2-membered heterocyclic radical or 5- or 6- membered heterocyclic ring;

$R^4$  is hydrogen or cyanate; and

$R^5$  is a negatively charged group.

3. The compound of claim 2, wherein

$R^1$  is hydrogen or methyl;

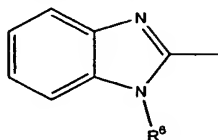
25  $R^2$  is lower alkyl;

$R^3$  is benzimidazole;

$R^4$  is a hydrogen; and

R<sup>5</sup> is alkoxycarbonyl or carboxyl.

4. The compound of claim 3, wherein R<sup>3</sup> is:



wherein R<sup>6</sup> is hydrogen, optionally substituted alkyl, halogen, amino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy, thiocarboxy, or carbamoyl.

5. The compound of claim 1, wherein:

R<sup>1</sup> is alkyl of 3 or more carbons;

R<sup>2</sup> is hydrogen, hydroxy, halo, amino alkylamino, dialkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy, thiocarboxy, carbamoyl, cyano, hydroxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, alkyl, alkenyl, alkynyl, aryl, 5- or 6- membered heterocyclic ring, or a fused 2-, 3-, or 4-membered heterocyclic radical;

R<sup>3</sup> is aryl, 5- or 6- membered heterocyclic ring, or a fused 2-, 3-, or 4-membered heterocyclic radical;

R<sup>4</sup> is a negatively charged group; and

R<sup>5</sup> is a negatively charged group.

6. The compound of claim 5, wherein

R<sup>1</sup> is propyl or butyl;

R<sup>2</sup> is lower alkyl;

R<sup>3</sup> is phenyl, a fused 2-membered heterocyclic radical or 5- or 6- membered heterocyclic ring;

R<sup>4</sup> is cyanate, 2-tetrazolyl, carboxyl, alkoxycarbonyl, carbamoyl, sulfonamido, or alkylsulfonamido; and

R<sup>5</sup> is cyanate, 2-tetrazolyl, carboxyl, alkoxycarbonyl, carbamoyl, sulfonamido, or alkylsulfonamido.

7. The compound of claim 6, wherein

R<sup>1</sup> is propyl or butyl;

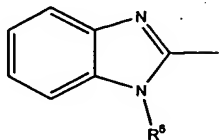
R<sup>2</sup> is lower alkyl;

$R^3$  is benzimidazole;

$R^4$  is lower alkoxycarbonyl or carboxyl; and

$R^5$  is lower alkoxycarbonyl or carboxyl.

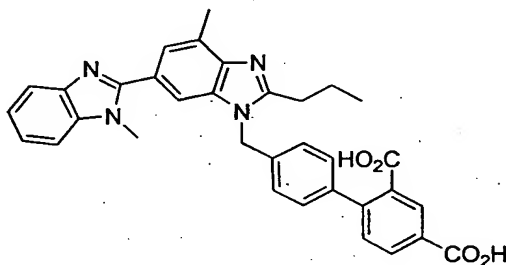
- 5 8. The compound of claim 7, wherein  $R^3$  is:



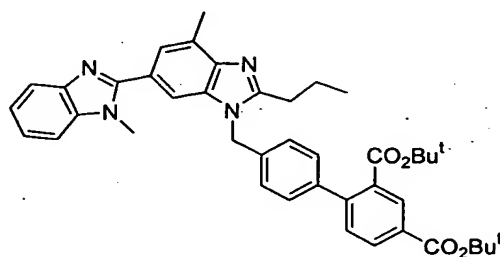
wherein  $R^6$  is hydrogen, optionally substituted alkyl, halogen, amino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy, thiocarboxy, or carbamoyl.

- 10 9. The compound of claim 8, wherein  $R^6$  is hydrogen or lower alkyl.

10. The compound of claim 9, wherein the compound has the structure:



11. The compound of claim 9, wherein the compound has the structure:



- 15 12. The compound of claim 1, wherein  $R^4$  and  $R^5$  independently are hydrogen or 2-tetrazolyl.

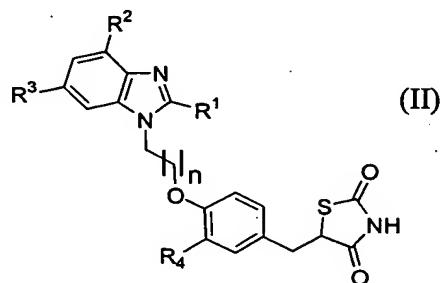
13. The compound of claim 1, wherein the compound at least partially activates a peroxisome proliferator-activated receptor.

14. The compound of claim 1, wherein the compound at least partially activates PPAR $\gamma$ .

5 15. The compound of claim 14, wherein the compound does not inhibit activity of the AT1 receptor.

16. The compound of claim 14, wherein the compound at least partially inhibits activity of the AT1 receptor.

17. A compound of the structure:



10

wherein R<sup>1</sup>, R<sup>2</sup>, and R<sup>3</sup> independently are hydrogen, hydroxy, halo, amino, alkylamino, dialkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxy, carbonyl, amido, alkoxy, thiocarboxy, carbamoyl, cyano, hydroxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, alkyl, alkenyl, alkynyl, aryl, 5- or 6- membered heterocyclic ring, or a fused 2-, 3-, or 4-membered heterocyclic radical;

15

n is 0 to 2; and

R<sup>4</sup> is hydrogen, cyanate, 2-tetrazolyl, carboxyl, alkoxy, carbonyl, amido, or sulfonamido.

20 18. The compound of claim 17, wherein

R<sup>1</sup> is hydrogen, lower alkyl or cyclolower alkylalkyl;

R<sup>2</sup> is hydrogen, lower alkyl, halogen, hydroxyl or NH<sub>2</sub>;

R<sup>3</sup> is phenyl, halogen, hydrogen, amino, alkoxy, hydroxyl, 5- or 6- membered heterocyclic ring, or a fused 2-4-membered heterocyclic radical; and

$R^4$  is hydrogen, cyanate, 2-tetrazolyl, carboxyl, alkoxycarbonyl, amido, or sulfonamido.

19. The compound of claim 18, wherein

$n$  is 1;

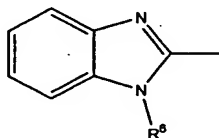
5  $R^1$  is hydrogen, methyl, ethyl or 4-cyclohexylbutyl;

$R^2$  is hydrogen, or methyl;

$R^3$  is phenyl, halogen, or benzimidazole; and

$R^4$  is loweralkoxycarbonyl or carboxyl.

20. The compound of claim 19, wherein  $R^3$  is:

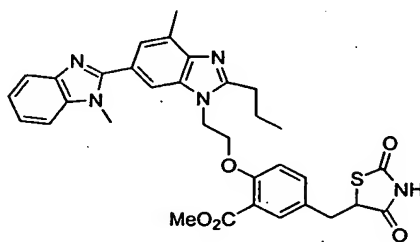


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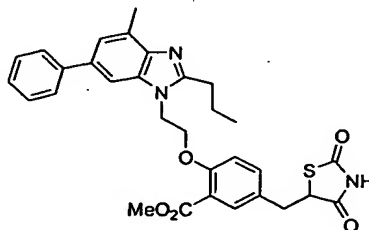
wherein  $R^6$  is hydrogen, optionally substituted alkyl, halogen, amino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy, thiocarboxy, or carbamoyl.

21. The compound of claim 20, wherein  $R^6$  is hydrogen or lower alkyl.

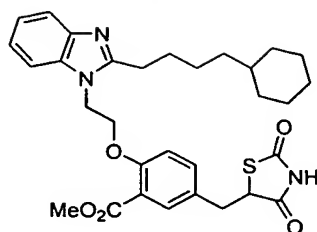
15 22. The compound of claim 21, wherein the compound has the structure:



23. The compound of claim 19, wherein the compound has the structure:



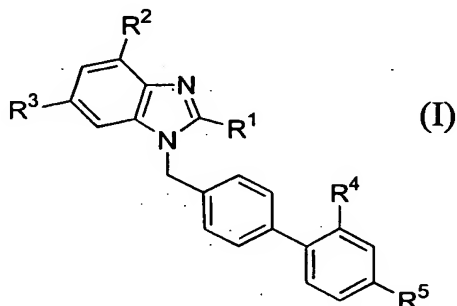
24. The compound of claim 19, wherein the compound has the structure:



25. The compound of claim 17, wherein the compound at least partially activates PPAR $\gamma$ .

26. A pharmaceutical composition for the treatment or prevention of an inflammatory or metabolic disorder in a mammal comprising:

(a) a compound having the structure:



wherein R<sup>1</sup>, R<sup>2</sup>, and R<sup>3</sup> independently are hydrogen, optionally substituted alkyl, cycloheteroalkyl, alkylheterocycloalkyl, aryl, halogen, heteroaryl, alkylheteroaryl, amino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy, thiocarboxy, carbamoyl, arylalkyl, heteroalkyl or heteroarylalkyl; and

R<sup>4</sup> and R<sup>5</sup> independently are hydrogen, cyanate, 2-tetrazolyl, carboxyl, alkoxycarbonyl, carbamoyl, sulfonamido, or alkylsulfonamido; and

(b) a pharmaceutically acceptable vehicle.

27. The pharmaceutical composition of claim 26, wherein:

R<sup>1</sup> is hydrogen, halogen, methoxy, hydroxyl, methyl, ethyl, or NH<sub>2</sub>;

R<sup>2</sup> is lower alkyl;

R<sup>3</sup> is phenyl, a fused 2-membered heterocyclic radical or 5- or 6- membered heterocyclic ring;

R<sup>4</sup> is hydrogen or cyanate; and

R<sup>5</sup> is a negatively charged group.

28. The pharmaceutical composition of claim 27, wherein

R<sup>1</sup> is hydrogen or methyl;

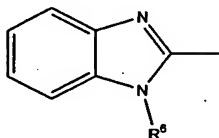
R<sup>2</sup> is lower alkyl;

R<sup>3</sup> is benzimidazole;

5 R<sup>4</sup> is a hydrogen; and

R<sup>5</sup> is alkoxycarbonyl or carboxyl.

29. The pharmaceutical composition of claim 28, wherein R<sup>3</sup> is:



10 wherein R<sup>6</sup> is hydrogen, optionally substituted alkyl, halogen, amino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy, thiocarboxy, or carbamoyl.

30. The pharmaceutical composition of claim 26, wherein:

R<sup>1</sup> is alkyl of 3 or more carbons;

15 R<sup>2</sup> is hydrogen, hydroxy, halo, amino alkylamino, dialkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy, thiocarboxy, carbamoyl, cyano, hydroxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, alkyl, alkenyl, alkynyl, aryl, 5- or 6- membered heterocyclic ring, or a fused 2-, 3-, or 4-membered heterocyclic radical;

20 R<sup>3</sup> is aryl, 5- or 6- membered heterocyclic ring, or a fused 2-, 3-, or 4-membered heterocyclic radical;

R<sup>4</sup> is a negatively charged group; and

R<sup>5</sup> is a negatively charged group.

31. The pharmaceutical composition of claim 30, wherein

R<sup>1</sup> is propyl or butyl;

25 R<sup>2</sup> is lower alkyl;

R<sup>3</sup> is phenyl, a fused 2-membered heterocyclic radical or 5- or 6- membered heterocyclic ring;

R<sup>4</sup> is cyanate, 2-tetrazolyl, carboxyl, alkoxycarbonyl, carbamoyl, sulfonamido, or alkylsulfonamido; and

R<sup>5</sup> is cyanate, 2-tetrazolyl, carboxyl, alkoxycarbonyl, carbamoyl, sulfonamido, or alkylsulfonamido.

32. The pharmaceutical composition of claim 31, wherein

R<sup>1</sup> is propyl or butyl;

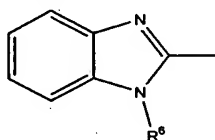
5 R<sup>2</sup> is lower alkyl;

R<sup>3</sup> is benzimidazole;

R<sup>4</sup> is lower alkoxycarbonyl or carboxyl; and

R<sup>5</sup> is lower alkoxycarbonyl or carboxyl.

33. The pharmaceutical composition of claim 32, wherein R<sup>3</sup> is:

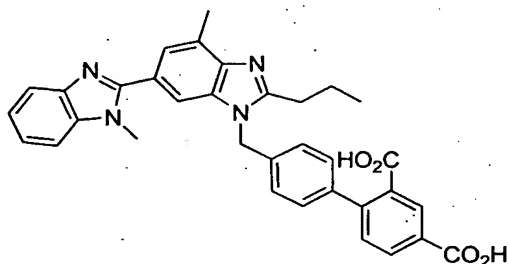


10

wherein R<sup>6</sup> is hydrogen, optionally substituted alkyl, halogen, amino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy, thiocarboxy, or carbamoyl.

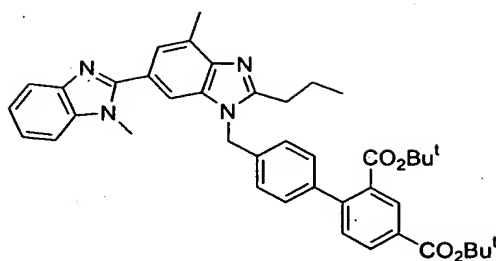
34. The pharmaceutical composition of claim 33, wherein R<sup>6</sup> is hydrogen or lower  
15 alkyl.

35. The pharmaceutical composition of claim 34, wherein the compound has the structure:



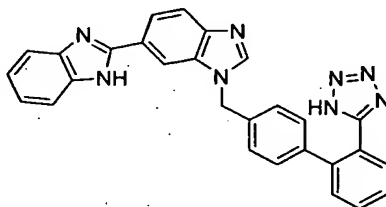
36. The pharmaceutical composition of claim 34, wherein the compound has the  
20 structure:





37. The pharmaceutical composition of claim 26, wherein  $R^4$  and  $R^5$  independently are hydrogen or 2-tetrazolyl.

38. The pharmaceutical composition of claim 37, wherein the compound has the structure:



39. The pharmaceutical composition of claim 26, wherein the compound at least partially activates  $PPAR\gamma$ .

40. The pharmaceutical composition of claim 39, wherein the compound does not inhibit activity of the AT1 receptor.

41. The pharmaceutical composition of claim 39, wherein the compound at least partially inhibits activity of the AT1 receptor.

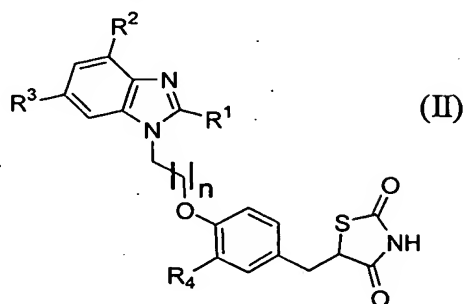
42. The pharmaceutical composition of claim 26, wherein the inflammatory or metabolic disorder is selected from the group consisting of type 2 diabetes, metabolic syndrome, and weight gain.

43. The pharmaceutical composition of claim 26, wherein the pharmaceutical composition is formulated for oral administration.

44. The pharmaceutical composition of claim 26, wherein the pharmaceutical composition is formulated for topical administration

45. A pharmaceutical composition comprising:

(a) a compound having the structure:



wherein  $R^1$ ,  $R^2$ , and  $R^3$  independently are hydrogen, optionally substituted  
5 alkyl, cycloheteroalkyl, alkylheterocycloalkyl, aryl, halogen, heteroaryl,  
alkylheteroaryl, amino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino,  
acyl, alkoxycarbonyl, amido, alkoxy, thiocarboxy, carbamoyl, arylalkyl, heteroalkyl  
or heteroarylalkyl;

$n$  is 0 to 2; and

10  $R^4$  is hydrogen, cyanate, 2-tetrazolyl, carboxyl, alkoxycarbonyl, amido, or  
sulfonamido; and

(b) a pharmaceutically acceptable vehicle.

46. The pharmaceutical composition of claim 45, wherein

$R^1$  is hydrogen, lower alkyl or cyclolower alkylalkyl;

15  $R^2$  is hydrogen, lower alkyl, halogen, hydroxyl or  $\text{NH}_2$ ;

$R^3$  is phenyl, halogen, hydrogen, amino, alkoxy, hydroxyl, 5- or 6- membered  
heterocyclic ring, or a fused 2-4-membered heterocyclic radical; and

$R^4$  is hydrogen, cyanate, 2-tetrazolyl, carboxyl, alkoxycarbonyl, amido, or  
sulfonamido.

20 47. The pharmaceutical composition of claim 46, wherein

$n$  is 1;

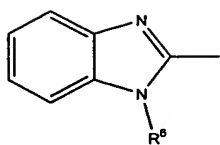
$R^1$  is hydrogen, methyl, ethyl or 4-cyclohexylbutyl;

$R^2$  is hydrogen, or methyl;

$R^3$  is phenyl, halogen, or benzimidazole; and

25  $R^4$  is loweralkoxycarbonyl or carboxyl.

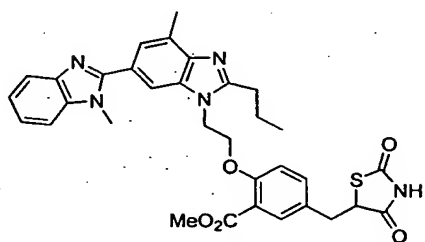
48. The pharmaceutical composition of claim 47, wherein  $R^3$  is:



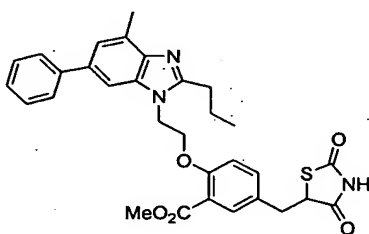
wherein  $R^6$  is hydrogen, optionally substituted alkyl, halogen, amino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy, thiocarboxy, or carbamoyl.

- 5 49. The pharmaceutical composition of claim 48, wherein  $R^6$  is hydrogen or lower alkyl.

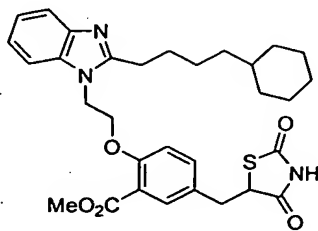
50. The pharmaceutical composition of claim 49, wherein the compound has the structure:



- 10 51. The pharmaceutical composition of claim 47, wherein the compound has the structure:



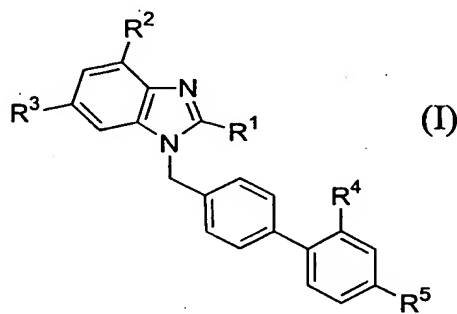
52. The pharmaceutical composition of claim 47, wherein the compound has the structure:



53. The pharmaceutical composition of claim 45 for the treatment or prevention of an inflammatory or metabolic disorder in a mammal.
54. The compound of claim 53, wherein the compound at least partially activates PPAR $\gamma$ .
- 5 55. The pharmaceutical composition of claim 54, wherein the inflammatory or metabolic disorder is selected from the group consisting of type 2 diabetes, metabolic syndrome, and weight gain.
56. The pharmaceutical composition of claim 45, wherein the pharmaceutical composition is formulated for oral administration.
- 10 57. The pharmaceutical composition of claim 45, wherein the pharmaceutical composition is formulated for topical administration
58. A method for treating or preventing an inflammatory or metabolic disorder in a mammal comprising administering to the mammal in need thereof, a therapeutically effective amount of a compound sufficient to at least partially activate a peroxisome proliferator-activated receptor (PPAR).
- 15 59. The method of claim 58, wherein the PPAR is PPAR $\gamma$  or a PPAR $\gamma$ -retinoid X receptor (PPAR $\gamma$ -RXR) heterodimer.
60. The method of claim 58, wherein the compound is administered orally.
61. The method of claim 58, wherein the compound is administered topically.
- 20 62. The method of claim 58, wherein the mammal is a human child, adolescent or adult.
63. The method of claim 58 wherein the therapeutically effective amount of the compound is sufficient to at least partially inhibit an activity of an angiotensin II type 1 receptor.
- 25 64. The method of claim 58, wherein the metabolic disorder is selected from the group consisting of type II diabetes, metabolic syndrome and weight gain.

65. The method of claim 58, further comprising treating at least one cardiovascular disorder associated with any component of the metabolic disorder, wherein the cardiovascular disorder is selected from the group consisting of steatohepatitis, neuropathy, nephropathy, retinopathy, retinal neovascularization, choroidal neovascularization, macular degeneration, retinal detachment, glaucoma, cataract, microangiopathy, atherosclerosis, arteriosclerosis, occlusive cerebrovascular disease, ischemic heart disease, occlusive coronary artery disease, occlusive peripheral vascular disease, stroke, peripheral arteriosclerosis, cerebral arteriosclerosis, coronary arteriosclerosis, hyperinsulinemia-induced sensory disorder, obesity, heart failure, congestive heart failure, myocardial infarction, myocardial fibrosis, angina pectoris, cerebral infarction, cardiomyopathy, renal disorders, glomerular nephritis, glomerulosclerosis, nephrotic syndrome, hypertensive nephrosclerosis, terminal renal disorders, thrombotic disease, thromboembolic disease, atheroma formation, atherogenesis.

66. The method of claim 58, wherein the compound has the structure:



wherein R<sup>1</sup>, R<sup>2</sup>, and R<sup>3</sup> independently are hydrogen, optionally substituted alkyl, cycloheteroalkyl, alkylheterocycloalkyl, aryl, halogen, heteroaryl, alkylheteroaryl, amino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy, thiocarboxy, carbamoyl, arylalkyl, heteroalkyl or heteroarylalkyl; and

R<sup>4</sup> and R<sup>5</sup> independently are hydrogen, cyanate or a negatively charged group.

67. The method of claim 66, wherein:

R<sup>1</sup> is hydrogen, halogen, methoxy, hydroxyl, methyl, ethyl, or NH<sub>2</sub>;

R<sup>2</sup> is lower alkyl;

R<sup>3</sup> is phenyl, a fused 2-membered heterocyclic radical or 5- or 6- membered heterocyclic ring;

R<sup>4</sup> is a hydrogen or cyanate; and

R<sup>5</sup> is a negatively charged group.

5 68. The method of claim 67, wherein

R<sup>1</sup> is hydrogen or methyl;

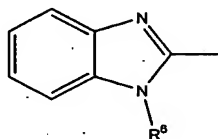
R<sup>2</sup> is lower alkyl;

R<sup>3</sup> is benzimidazole;

R<sup>4</sup> is a hydrogen; and

10 R<sup>5</sup> is alkoxycarbonyl or carboxyl.

69. The method of claim 68, wherein R<sup>3</sup> is:



wherein R<sup>6</sup> is hydrogen, optionally substituted alkyl, halogen, amino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy, 15 thiocarboxy, or carbamoyl.

70. The method of claim 66, wherein the therapeutically effective amount of the compound is sufficient to at least partially inhibit an activity of an angiotensin II type 1 receptor.

71. The method of claim 70, wherein:

20 R<sup>1</sup> is alkyl of 3 or more carbons;

R<sup>2</sup> is hydrogen, hydroxy, halo, amino alkylamino, dialkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy, thiocarboxy, carbamoyl, cyano, hydroxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, alkyl, alkenyl, alkynyl, aryl, 5- or 6- membered 25 heterocyclic ring, or a fused 2-, 3-, or 4-membered heterocyclic radical;

R<sup>3</sup> is aryl, 5- or 6- membered heterocyclic ring, or a fused 2-, 3-, or 4-membered heterocyclic radical;

R<sup>4</sup> is a negatively charged group; and

R<sup>5</sup> is a negatively charged group.

72. The method of claim 71, wherein

R<sup>1</sup> is propyl or butyl;

R<sup>2</sup> is lower alkyl;

5 R<sup>3</sup> is phenyl, a fused 2-membered heterocyclic radical or 5- or 6- membered heterocyclic ring;

R<sup>4</sup> is cyanate, 2-tetrazolyl, carboxyl, alkoxycarbonyl, carbamoyl, sulfonamido, or alkylsulfonamido; and

R<sup>5</sup> is cyanate, 2-tetrazolyl, carboxyl, alkoxycarbonyl, carbamoyl, sulfonamido, or alkylsulfonamido.

10 73. The method of claim 72, wherein

R<sup>1</sup> is propyl or butyl;

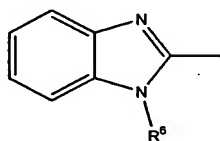
R<sup>2</sup> is lower alkyl;

R<sup>3</sup> is benzimidazole;

R<sup>4</sup> is lower alkoxycarbonyl or carboxyl; and

15 R<sup>5</sup> is lower alkoxycarbonyl or carboxyl.

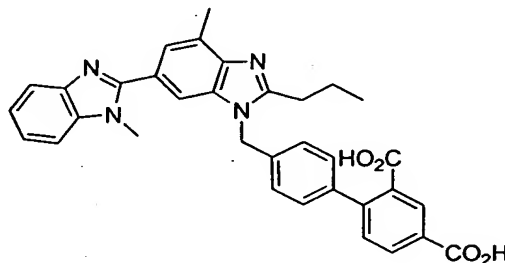
74. The method of claim 73, wherein R<sup>3</sup> is:



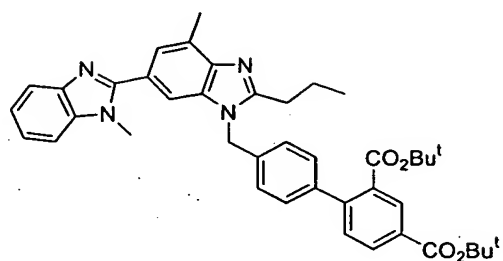
wherein R<sup>6</sup> is hydrogen, optionally substituted alkyl, halogen, amino, alkylthio, 20 alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy, thiocarboxy, or carbamoyl.

75. The method of claim 74, wherein R<sup>6</sup> is hydrogen or lower alkyl.

76. The method of claim 75, wherein the compound has the structure:

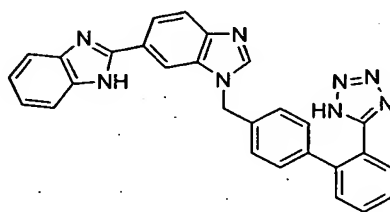


77. The method of claim 75, wherein the compound has the structure:

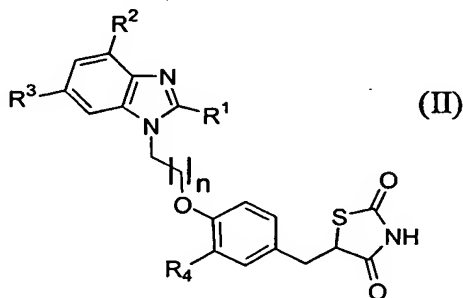


78. The method of claim 66, wherein  $R^4$  and  $R^5$  independently are hydrogen or 2-tetrazolyl.

5 79. The method of claim 78, wherein the compound has the structure:



80. The method of claim 58, wherein the compound has the structure:



10 wherein  $R^1$ ,  $R^2$ , and  $R^3$  independently are hydrogen, hydroxy, halo, amino, alkylamino, dialkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxy, thiocarbonyl, carbamoyl, cyano, hydroxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, alkyl, alkenyl, alkynyl, aryl, 5- or 6- membered heterocyclic ring, or a fused 2-, 3-, or 4-membered heterocyclic radical;

15 n is 0 to 2; and

$R^4$  is hydrogen, cyanate, 2-tetrazolyl, carboxyl, alkoxy, carbonyl, amido, or sulfonamido.



81. The method of claim 80, wherein

$R^1$  is hydrogen, lower alkyl or cyclolower alkylalkyl;

$R^2$  is hydrogen, lower alkyl, halogen, hydroxyl or  $NH_2$ ;

$R^3$  is phenyl, halogen, hydrogen, amino, alkoxy, hydroxyl, 5- or 6- membered  
5 heterocyclic ring, or a fused 2-4-membered heterocyclic radical; and

$R^4$  is hydrogen, cyanate, 2-tetrazolyl, carboxyl, alkoxycarbonyl, amido, or  
sulfonamido.

82. The method of claim 81, wherein

$n$  is 1;

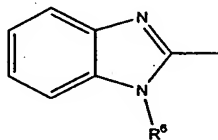
10  $R^1$  is hydrogen, methyl, ethyl or 4-cyclohexylbutyl;

$R^2$  is hydrogen, or methyl;

$R^3$  is phenyl, halogen, or benzimidazole; and

$R^4$  is loweralkoxycarbonyl or carboxyl.

83. The method of claim 82, wherein  $R^3$  is:

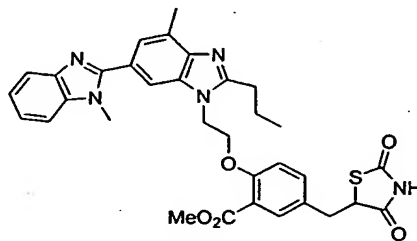


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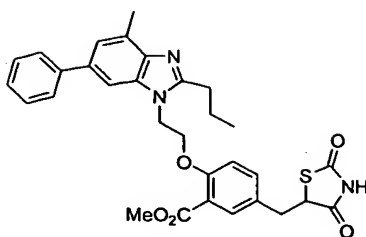
wherein  $R^6$  is hydrogen, optionally substituted alkyl, halogen, amino, alkylthio,  
alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxycarbonyl, amido, alkoxy,  
thiocarboxy, or carbamoyl.

84. The method of claim 83, wherein  $R^6$  is hydrogen or lower alkyl.

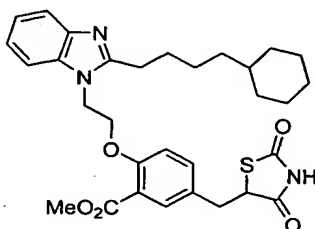
20 85. The method of claim 84, wherein the compound has the structure:



86. The method of claim 82, wherein the compound has the structure:



87. The method of claim 82, wherein the compound has the structure:



88. A method of screening a compound for capability to treat or prevent an inflammatory or metabolic disorder in a mammal, the method comprising:

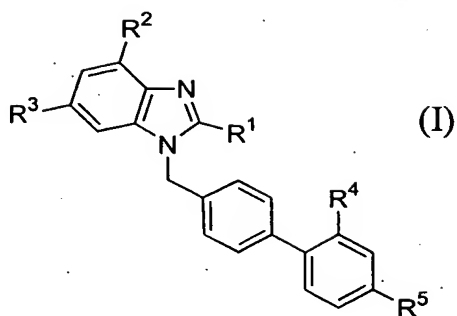
- (a) identifying a compound as at least partially activating a peroxisome proliferator-activated receptor (PPAR);
- (b) identifying the compound as at least partially inhibiting an activity of an angiotensin II type 1 receptors; and

(c) selecting the compound as capable of treating or preventing an inflammatory or metabolic disorder.

89. The method of claim 88, wherein the PPAR is PPAR $\gamma$ .

90. The method of claim 88, further comprising selecting a compound that does not cause, promote, or aggravate at least one of fluid retention, peripheral edema, pulmonary edema, and congestive heart failure in the mammal.

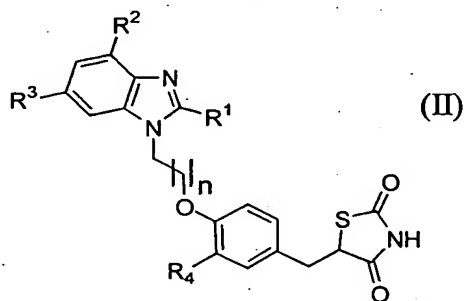
91. The method of claim 88, wherein the compound has the structure:



wherein  $R^1$ ,  $R^2$ , and  $R^3$  independently are hydrogen, hydroxy, halo, amino alkylamino, dialkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxy, thiocarboxy, carbamoyl, cyano, hydroxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, alkyl, alkenyl, alkynyl, aryl, 5- or 6- membered heterocyclic ring, or a fused 2-, 3-, or 4-membered heterocyclic radical;

$R^4$  and  $R^5$  independently are hydrogen, cyanate, or a negatively charged group.

92. The method of claim 88, wherein the compound has the structure:



wherein  $R^1$ ,  $R^2$ , and  $R^3$  independently are hydrogen, hydroxy, halo, amino alkylamino, dialkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonylamino, acyl, alkoxy, thiocarboxy, carbamoyl, cyano, hydroxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, alkyl, alkenyl, alkynyl, aryl, 5- or 6- membered heterocyclic ring, or a fused 2-, 3-, or 4-membered heterocyclic radical;

$n$  is 0 to 2; and

$R^4$  is hydrogen, cyanate, 2-tetrazolyl, carboxyl, alkoxy, carbonyl, amido, or sulfonamido.